Remarks

Claim Objections

Claims 18 and 19 have been amended to refer to "the" instead of "a", as suggested by the examiner.

Rejection Under 35 U.S.C. § 112, first paragraph (written description)

Claims 1, 3, 6, 7, 13, and 15-24 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed.

The examiner's rejection is not understood. Applicant has identified those portions of the specification that make clear that the polymer may be therapeutic, or it may be used to deliver therapeutic agent, which the examiner appears to agree with.

As claim 5 as originally filed stated ""wherein the polymers are selected from the group consisting of solid matrices, porous matrices.....". This language implied, but omitted, that the polymers were in the form of these materials since none of these materials are polymers *per se*, but polymeric materials, i.e., a hydrogel is formed of polymer; a microparticles is formed of polymer. Claim 1 and claims dependent thereon have been amended to clarify this point. The examiner's attention is drawn to page 12, for example, for a discussion of the forms and uses of the polymers. Support for the phrase "polymeric materials" is found at page 13, line 2, and at page 3, lines 17-23, and abstract, where it is explicitly stated "application of polymeric material alone or in combination with bioactive agents or cells". See also page 4, line 20; page 8, lines 17-28; and page 14, lines 11-16; 22-28.

Rejections Under 35 U.S.C. § 102

Claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,585,716 by Altman ("the '716 patent"). Claims 1, 3, 6, 7, 15-19, 21-23, 25, 34, 36 and 37 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,102,887 by Altman ("the '887 patent"). Claims 1, 3, 6, 7, 14-16, 18, 20-24, 32 and 34-37 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent"). Applicant respectfully traverses these rejections.

The Claimed Invention

The claims are drawn to a method. The method requires the following steps:

(1) penetrating into by cutting or removal of tissue the endomural zone of a tissue,

(2) with a means for delivery of a therapeutic, prophylactic or diagnostic agent,

(3) delivering the therapeutic, prophylactic or diagnostic agent into the stie of cutting or tissue removal,

(4) where the agent is in a form for local delivery of an effective amount of the therapeutic, prophylactic or diagnostic agent,

(5) where the agent is delivered in a polymeric material.

The examiner is correct that the heart includes an endomural zone, between the outer layer and the inner lumen. This is how the endomural zone is defined in applicant's specification.

Spinal cord is not a tissue, but many nerves that are "packaged" together. This does not fit into the definition at page 5 of tissue components which are organized into organs, requiring

multiple integrated and interactive tissue components. The endomural zone is defined at page 6 as a region in an organ.

Accordingly, the examiner is correct that there is an endomural zone within the tissue forming the heart; the examiner is not correct to the extent it is alleged that the spinal cord has an endoluminal zone.

Analysis

The '716 patent

The '716 patent describes methods for treating the human heart. A guide catheter is placed in the venous portion of a patient's vasculature and extends until the vena cava and coronary sinus. A drug delivery catheter is inserted inside the guide catheter and extends beyond the guide catheter so that the tip enters the cardiac vein and extends to the posterior vein. The tip contains a penetrating element, such as a curved or helical needle, that is selectively extended into the wall of the vein and into the myocardium. Therapeutic agents are injected into the myocardium, through the needle (col. 4, lines 5-19 and Figure 1). The guide catheter contains an occluding mechanism. The venous flow path is shut off by occluding the coronary ostium with the occluding mechanism. This stops the natural blood flow from the myocardium into the vein, thereby preventing the therapeutic agents from being flushed out of the myocardium in the course of normal blood flow. (col. 4, lines 20-47)

The '716 patent does not disclose forming a void, cavity, containment space or reservoir area in the endomural zone as required by amended claims 1, 15 and 25. The '716 patent merely uses a catheter which is inserted between cells into the heart tissue for delivery of drug to the

vasculature within the heart. This is a pre-existing structure. There is no teaching to create a new void, cavity, containment space or reservoir area by cutting or other means permanently removing the tissue. Insertion of a needle or catheter does not create a void as claimed, but merely pushes aside tissue which refills the temporary displacement upon removal of the device. Catheters and needles do not cut or remove tissue; they simply displace it.

The examiner states that because applicant has stated that needles or catheters can be used, the device in Altman must perform the same function. This is not the case. A needle or cathether, of an appropriate bore size, can be used to remove tissue; a needle of a smaller size, can be used to displace tissue, not remove tissue.

Altman does not create a void into which a polymeric material is implanted. Altman injects into the tissue a dispersion of particles for drug delivery. Altman disperses particles throughout the tissue. This is very clear by reference to col. 4. A catheter is used to pass through blood vessels into the inferior vena cava, from which a needle (note the significantly smaller size) is used to inject (and the use of the word "inject", line 18) particles into the myocardium. Steps have to then be taken so that the particles are retained (line 20 of col. 4, see also col. 5, lines 16-38) - if there was void or containment region created, no additional steps to retain the particles at the site would be required. This statement alone differentiates the method of the '716 patent from the claimed method. See also col. 5, lines 56-60.

In summary, Altman's method is not the same as that of applicant based on at least two differences:

Altman does not use a means for cutting or creating a void;

Altman does not put into the void a polymeric material which is retained within the void.

Altman instead injects into the tissue, not removing any tissue, which causes problems with retention, since the tissue has merely been pushed aside by the needle, and therefore sequeezes back to its previous shape when the needle is withdrawn, trying to expel the drug.

Altman also does not disclose projectile means, expansile cutter means, or a void filling material.

Therefore, claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are novel over the '716 patent.

The '887 patent

The '887 patent describes a steerable catheter with a deployable penetrating element, such as a helical or straight needle, for administration of drugs to the heart (col. 3, lines 9-22). Agents can be delivered in microformulations such as microspheres, nanoparticles or polymers. The claims, as amended require creating a void, cavity, containment space or reservoir area in the endoluminal zone by cutting or removal of tissue. The '887 patent merely uses a catheter with a distensible needle for delivery of drugs to the myocardium of the heart. There is no teaching to create a new void, cavity, containment space or reservoir area by cutting or any other means which permanently remove the tissue. As discussed above with respect to the '716 patent, insertion of a needle or catheter does not create a void as claimed, but merely pushes aside tissue which refills the temporary displacement upon removal of the device. Catheters and needles do not cut or remove tissue; they simply displace it.

Col. 9, lines 20-52 discloses an expanding prong *fixation* system, which may be used to *stabilize* the needle, *not* to create a void, cavity, containment space or reservoir as required by independent claims 1, 15 and 25. Merriam-Webster defines "void" as "not occupied" or "containing nothing". Merriam-Webster also defines "cavity" as "an unfilled space within a mass" (*see* definition attached). The instant claims require the formation of such an "*unfilled* space", into which the therapeutic, prophylactic or diagnostic agent is delivered. Although the prong fixation system disclosed in the '887 patent is able to penetrate body tissue, this merely creates a cut in the tissue which is *occupied*, or *filled* with the prongs. The fixation system is designed to stay in place as the agent is delivered. The '887 patent does not disclose retracting the prongs prior to delivery of an agent. Thus, the prongs of the fixation system disclosed in the '887 patent do not create a void, cavity, containment space or reservoir into which the agent is delivered.

In col. 2, Altman makes clear that the prior art describes a variety of means for infusing the heart. All of these are referred to as penetrating needles or catheters, and that his improvement is the addition of steering and fixation means. The summary reinforces the argument that the delivery is by injection into the tissue NOT creation of a void into which polymeric material is implanted. IF the needle were removing tissue, then there would have to be some means to dispose of the tissue prior to using the same needle to inject drug. There is none. IF the needle were used to create a void, the lumen of the needle would be filled with tissue; no drug could pass through into the space. However, this clearly does not happen because

no tissue is removed, no void is created. Therefore, Altman '887 does not anticipate the claimed methods and claims 1, 3, 6, 7, 15-18, 19, 21-23, 25, 34, 36 and 37 are novel over the '887 patent.

The '370 patent

The '370 patent discloses a method and device for delivery of growth factors to an ischemic region in the heart. The '370 patent emphasizes the importance of navigating the catheter to the site of the ischemic regions (see col. 4, lines 25-40). The device is a catheter that contains sensors to determine the position of the catheter with respect to the heart wall (col. 12, lines 10-28). When the device is in place, the needle is placed inside the heart wall and the growth factors are delivered (see e.g. col. 12, lines 40-49 and col. 13, lines 39-50 and col. 14, lines 3-11). The growth factors may be administered in a solution or a capsule (see col. 15, lines 14-20).

As discussed above with respect to the '716 and '887 patents, the '370 patent does not disclose forming a void, cavity, containment space or reservoir area in the **endomural** zone, as required by amended claims 1, 15 and 25. The '370 patent merely uses a catheter for delivery of drug to the vasculature within the heart.

As discussed above, none of these reference disclose creating a void and then filling it.

Moreover, none of the references disclose creating a void in the endomural zone. The examiner has stated that the region that is treated must be the endomural zone, but has provided no evidence that this would inherently be the case. Inherence requires more than the mere possibility; it must be the case. All of these methods are designed to deliver drug to a particular

area of the heart, usually one that has been damaged due to ischemia. There is no indication that this region would be, or even principally be, the endomural zone.

In summary, the prior art does not anticipate the claims because it does not teach creation of a void; filling of a void with a polymeric material.

Should the examiner enter the proposed amendment, none of these references would also anticipate because the claims no longer encompass delivery of micro or nanoparticles.

Rejection Under 35 U.S.C. § 103

Claims 13 and 33 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 6,585,716 by Altman ("the '716 patent") or U.S. Patent No. 6,102,887 by Altman ("the 887 patent) or U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent"), in view of Benjamin and McMillan, *Circ. Res.*, 83:117-132 (1988) ("Benjamin and McMillan"). Claim 31 was rejected under 35 U.S.C. § 103(a) as obvious over Brosamle, *et al.*, The Journal of Neuroscience, 20(21):8061-68 ("Brosamle") in view of U.S. Patent No. 6,585,716 by Altman ("the '716 patent") or U.S. Patent No. 6,102,887 by Altman ("the 887 patent) or U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent"). Applicant respectfully traverses these rejections.

The claims, Altman '716, Altman '887 and Haim have been discussed above. The claimed method requires creation of a void and filing of the void with a polymeric material. Altman and Haim describe displacement and the use of remedial measures involving physical displacement to keep the injected drugs within the site of injection. This teaches away from what applicant claims.

The combination of the '716, '887, or '370 patents with Benjamin

As noted above, none of the '716, '887 or '370 patents disclose a means for forming a void, cavity, containment space or reservoir area in the endomural zone by cutting or removing tissue. Additionally, the '370 patent does not disclose including a void filling material or implant in the device.

Benjamin is a general reference about heat shock proteins and some of their roles. Benjamin does not cure the deficiencies of the '716, '887, and '370 patents. The combination of these references still does not disclose or suggest delivering heat shock proteins, stress response proteins, and inducers of heat shock or stress response proteins into a void, cavity, containment space or reservoir area created by cutting or removal of tissue as defined by claim 13. Additionally, the combination of Benjamin with the '716, '887, and '370 patents does not disclose a kit containing a void filling material or implant in a form suitable for local administration, as required by claim 33.

Claim 31

Claim 31 is device claim that depends from claim 15 and further defines the device as being suitable for nerve regeneration.

The combination of Brösamle with Altman '716, Altman '887, or Haim

As noted above, the '716, '887 and '370 patents do not disclose forming a void, cavity, containment space or reservoir area in the endomural zone by cutting or removing tissue, as required by claim 31. Brösamle describes administering an antibody to the spinal cord to promote regeneration. Brösamle does not cure the deficiencies of the '716, '887 or '370 patents.

Brösamle does not disclose a device with means for for creating a void, cavity, containment space or reservoir area. Therefore the combination of Brösamle with the '716, '887, or '370 patents does not make claim 31 obvious.

Allowance of claims 1, 3, 6, 7, 13, 15-25, 28, 29, 31-33 and 35-37 is respectfully solicited.

Respectfully submitted,

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